Paragraph [0033], line 12
change "lip" to "collar"

In the Claims:

1. (currently amended) A microfluidic system comprising:

a first substrate having at least one microfluidic through-hole between first and second surfaces of the first substrate, the through-hole having a cross-section sufficient to retain a liquid therein; and

<u>a first substrate having at least one peak protruding from the second surface of the first substrate, the at least one through-hole of the first substrate being in fluid communication with the tip of the at least one peak.</u>

a second substrate having at least one microfluidic through-hole in a predetermined proximate spaced position and alignment with the at least one microfluidic through-hole of the first substrate, the at least one through-hole of the second substrate operable to retain the liquid displaced from the at least one through-hole of the first substrate thereto.

2. (original) The microfluidic system, as set forth in claim 1, further comprising means for displacing a liquid retained in the at least one through-hole of the first substrate to the at least one through-hole of the second substrate.

3. (original) The microfluidic system, as set forth in claim 1, further comprising means for aligning the at least one microfluidic through-hole of the first and second substrates.

4. (original) The microfluidic system, as set forth in claim 1, further comprising a physically driven force generated by meniscus contact between the liquids for displacing a liquid retained in the at least one through-hole of the first substrate to the at least one through-hole of the second substrate.

5. (original) The microfluidic system, as set forth in claim 1, further comprising a chemically driven force generated by meniscus contact between the liquids for displacing a liquid retained in the at least one through-hole of the first substrate to the at least one through-hole of the second substrate.

6. (original) The microfluidic system, as set forth in claim 1, further comprising a physically driven force generated by a pressure differential along the thickness of the substrates for displacing a liquid retained in the at least one through-hole of the first substrate to the at least one through-hole of the second substrate.

7. (original) The microfluidic system, as set forth in claim 1, further comprising a physically driven force generated by an electrokinetic differential along the thickness of the substrates for displacing a liquid retained in the at least one through-hole of the first substrate to the at least one through-hole of the second substrate.

8. (original) The microfluidic system, as set forth in claim 1, further comprising a spacer disposed between the first and second substrates and operable to maintain an air gap in the predetermined spaced position between the first and second substrates.

9. (original) The microfluidic system, as set forth in claim 1, wherein the first and second substrates each further comprises hydrophobic upper and lower surfaces.

10. (original) The microfluidic system, as set forth in claim 1, wherein the at least one microfluidic through-hole of the second substrate comprises a tapered inner wall.

11. (original) The microfluidic system, as set forth in claim 1, wherein the at least one microfluidic through-hole of the first substrate comprises a tapered inner wall.

12. (original) The microfluidic system, as set forth in claim 1, wherein the at least one microfluidic through-holes of the first and second substrates each comprises a tapered inner wall.

13. (cancelled)

14. (currently amended) The microfluidic system, as set forth in claim ~~13~~ 1, wherein the at least one peak of the first substrate is operable to be at least partially accommodated within the at least one microfluidic through-hole of the second substrate to make contact with the liquid retained therein.

15. (original) The microfluidic system, as set forth in claim 1, wherein the first substrate further comprises a collar surrounding the opening of the at least one microfluidic through-hole in the second surface.

16. (cancelled)

17. (cancelled)

18. (cancelled)

19. (original) The microfluidic system, as set forth in claim 1, wherein the first and second substrates comprise a hydrophobic coating on the first and second surfaces thereof except for a predetermined distance from each through-hole opening.

20. (original) The microfluidic system, as set forth in claim 19, wherein the first and second substrates further comprise a non-hydrophobic surface between the hydrophobic coating and the through-hole openings.

21. (original) The microfluidic system, as set forth in claim 1, further comprising a plurality of microfluidic through-holes in each of the first and second substrates.

22. (currently amended) A microfluidic system comprising:

a first substrate having an array of microfluidic through-holes having a first predetermined geometry between first and second surfaces of the first substrate, the through-holes operable to retain a liquid therein by physical and/or chemical fluidic forces;

<u>a first substrate having at least one peak protruding from the second surface of the first substrate, the at least one through-hole of the first substrate being in fluid communication with the tip of the at least one peak.</u>

a second substrate having an array of microfluidic through-holes having a second predetermined geometry and in a predetermined proximate spaced position and alignment with the microfluidic through-holes of the first substrate, the through-holes of the second substrate operable to receive and retain a liquid retained and then displaced from the through-holes of the first substrate to the through-holes of the second substrate, the

through-holes operable to retain the liquid by physical and/or chemical fluidic forces; and

an applied force operable to displace the liquid retained in the through-holes of the first substrate to the through-holes of the second substrate.

23. (original) The microfluidic system, as set forth in claim 22, further comprising means for aligning the microfluidic through-holes of the first and second substrates.

24. (original) The microfluidic system, as set forth in claim 22, wherein applied force comprises a force generated by meniscus contact between the liquids in the through-holes in the first and second substrates.

25. (original) The microfluidic system, as set forth in claim 22, wherein the applied force comprises a physically driven force generated by a pressure differential along the thickness of the substrates.

26. (original) The microfluidic system, as set forth in claim 22, wherein the applied force comprises a physically driven force generated by an electrokinetic differential along the thickness of the substrates.

27. (original) The microfluidic system, as set forth in claim 22, further comprising a spacer disposed between the first and second substrates and operable to maintain an air gap in the predetermined spaced position between the first and second substrates.

28. (original) The microfluidic system, as set forth in claim 22, wherein the first and second substrates each further comprises hydrophobic upper and lower surfaces.

29. (original) The microfluidic system, as set forth in claim 22, wherein the first and second geometries of the through-holes are the same.

30. (original) The microfluidic system, as set forth in claim 22, wherein the first and second geometries of the through-holes are different.

31. (original) The microfluidic system, as set forth in claim 22, wherein the second predetermined geometries of the microfluidic through-holes of the second substrate comprises a tapered inner wall.

32. (original) The microfluidic system, as set forth in claim 22, wherein the first and second predetermined geometries of the microfluidic through-holes of the first and second substrates comprise a tapered inner wall.

33. (original) The microfluidic system, as set forth in claim 22, wherein the first and second predetermined geometries of the microfluidic through-holes of the first and second substrates comprise a conically tapered inner wall.

34. (original) The microfluidic system, as set forth in claim 22, wherein the first and second predetermined geometries of the microfluidic through-holes of the first and second substrates comprise a pyramidally tapered inner wall.

35. (original) The microfluidic system, as set forth in claim 22, wherein the microfluidic through-holes of the first substrate each reaching the second surface at a peak protruding therefrom.

36. (original) The microfluidic system, as set forth in claim 33, wherein each peak of the first substrate is operable to be at

least partially accommodated within the microfluidic through-hole of the second substrate to make contact with the liquid retained therein.

37. (original) The microfluidic system, as set forth in claim 22, wherein the first substrate further comprises a collar surrounding the opening of each microfluidic through-hole and protruding beyond the second surface.

38. (cancelled)

39. (cancelled)

40. (original) The microfluidic system, as set forth in claim 22, wherein the first and second substrates comprise a hydrophobic coating on the first and second surfaces thereof except for a predetermined distance from each through-hole opening.

41. (cancelled)

42. (original) The microfluidic system, as set forth in claim 22, further comprising a third substrate disposed adjacent the second substrate and having a plurality of microwells disposed in a surface of the substrate facing the second substrate, the microwells operable to receive the liquid displaced from the microfluidic through-holes of the first substrate to the microfluidic through-holes of the second substrate and then to the microwells.

43. (original) The microfluidic system, as set forth in claim 42, further comprising a channel defined between the second and third substrates operable to guide the liquid from the microfluidic thorough-holes of the second substrate to the microwells in the third substrate.

44. (original) The microfluidic system, as set forth in claim 22, wherein the through-holes in the first substrate are in in-line alignment with the through-holes in the second substrate.

45. (original) The microfluidic system, as set forth in claim 22, wherein the through-holes in the first substrate are in offset alignment with the through-holes in the second substrate.

46. (original) The microfluidic system, as set forth in claim 45, further comprising a channel defined in the predetermined space between the first and second substrates and in fluid communication with selected through-holes of the first and second substrates.

47. (original) A method of transferring liquids between first and second substrates, comprising:

loading a first liquid into a plurality of microfluidic through-holes disposed in the first substrate, the first liquid being retained in the through-holes;

loading a second liquid into a plurality of microfluidic through-holes disposed in the second substrate, the second liquid being retained in the through-holes; and

transferring the first liquid in the first substrate into the through-holes of the second substrate induced by meniscus contact between the first and second liquids and an applied force.

48. (original) The method, as set forth in claim 47, wherein transferring the first liquid comprises creating an electrical field differential across the first and second substrates.

49. (original) The method, as set forth in claim 47, wherein transferring the first liquid comprises creating a pneumatic differential across the first and second substrates.

50. (original) The method, as set forth in claim 47, further comprising transferring the liquid in the through-holes of the second substrate to microwells disposed in a third substrate.

51. (original) The method, as set forth in claim 47, further comprising positioning the first and second substrates so that the through-holes therein are in alignment with one another.

52. (original) The method, as set forth in claim 47, further comprising positioning the first and second substrates so that a fluid-conducting channel is formed between the first and second substrates, the channel being in fluid communication with at least selected ones of through-holes in the first and second substrates.

53. (original) The method, as set forth in claim 47, wherein loading the through-holes of the first and second substrates comprises immersing the first and second substrates into the respective first and second liquids.

54. (original) The method, as set forth in claim 53, wherein loading the through-holes of the first and second substrates comprises:

immersing the first and second substrates into respective containers containing the respective first and second liquids; and

evacuating gases from the respective containers.

55. (original) A method comprising:

loading a first test sample into a plurality of microfluidic through-holes disposed in the first substrate, the first test samples being retained in the through-holes;

loading a reagent into a plurality of microfluidic through-holes disposed in the second substrate, the reagent being retained in the through-holes; and

transferring the reagent in the second substrate into the through-holes of the first substrate induced by an applied force;

positioning and aligning a third substrate having a plurality of microfluidic through-holes with the microfluidic through-holes of the first substrate and forming a fluid-conducting channel in fluid communication with the through-holes of the first and third substrates between the first and third substrates; and

flushing the test sample reagent mixture in the through-holes of the first substrate with a washing liquid introduced into the through-holes of the third substrate.

56. (original) The method, as set forth in claim 55, wherein transferring the reagent comprises creating an electrical field differential across the first and second substrates.

57. (original) The method, as set forth in claim 55, wherein transferring the reagent comprises creating a pneumatic differential across the first and second substrates.

58. (original) The method, as set forth in claim 55, further comprising transferring the test sample and reagent in the

through-holes of the first substrate to microwells disposed in a fourth substrate.

59. (original) A method of preparing samples comprising:

introducing an array of samples into a first substrate retained thereby by various fluid imbalance forces;

positioning a second substrate adjacent the first substrate and receiving an array of spots of samples therefrom onto the second substrate;

positioning a third substrate adjacent the second to further create another array of samples on the second substrate;

repeating the above step with additional substrates to build a library of samples on the second substrate; and

positioning and aligning the second substrate with the library of samples adjacent to an assay reagent substrate having an array of assay reagents.

60. (original) The method, as set forth in claim 59, further comprising transferring the samples to the second substrate by applying an electrical field differential across the first and second substrates.

61. (original) The method, as set forth in claim 59, further comprising transferring the samples to the second substrate by a pneumatic differential across the first and second substrates.

62. (original) The method, as set forth in claim 47, wherein, un-loading the through holes of the first and second substrates comprises blowing a gas jet against the through-holes.

Response to Arguments

Examiner rejected claims 13-18 and 35-39 under 35 U.S.C. 112 due to failing to comply with the enablement requirements. Regarding claims 13,14,35 and 36, the specification does not appear to

teach the incorporation of a protruding peak structure within the claimed apparatus.

Specification changes are made as proposed in the specification amendments to care of this issue.

Examiner mentions regarding claims 15 and 37, the specification does not appear to mention the incorporation of a collar structure.

The word "lip" was used in the previous specification, which is changed to "collar" in the above specification amendments to take care of this issue.

Claims 1-8, 21, 22 and 24-27, 29, 30 and 42-46 are rejected under 35 U.S.C. 102(b) as being anticipated by Demers (U.S. Pat No. 5,879,632 A). It is claimed that the design is structurally no different from the prior art.

In order to further distinguish the structure from the prior art, additional feature of a protrusion on the second surface is included as part of the independent claims. This feature allows the interpenetration of the fluid meniscus of the first substrate into the fluid meniscus of the second substrate (Paragraph 0032). In Demers patent, the structure is such that a single meniscus or no meniscus is used and the structure cannot be used to intermix two meniscus in which case the interpenetrating protrusion structural feature is essential. This feature is not obvious since the unrecognized problem of making two meniscus to come in contact that otherwise would not if the surfaces are flat without a protrusion. This unexpected result allows combining of fluids in arrays. The air gap formed in Demers Patent by the

apportionment chamber (1405 A) between the first and second substrates does not allow intermixing of meniscus and is not the appropriate feature.

The description of this feature is included in the specification paragraphs [0030] and [0031] as described by the specification amendments.

Claims 9, 19, 20, 28, 40 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Demers in view of Jedrzejewski et al.

The additional structural feature inclusion presented above combined with the incorporation of the hydrophobic upper and lower surfaces, constitutes a novel and non obvious invention over the prior art. Additionally, the protrusion, 18 in Fig. 1 and 1 A is in fluid communication with a through-hole 20. This feature is non obvious where the through-hole and the protrusion are connected to each other. A simple protrusion without the thorough-hole will not allow mixing of two meniscus as well as suspension of the meniscus in the through-hole. This feature is novel over the prior art.

Fisher et al. (US Patent 6,689,323 B2) disclose a structure in Fig. 1C to move the meniscus, 102 using a movable pin, 108 which requires tight guides, 16 for motion which is structurally different from non moving meniscus in the current application. Bass (US Patent 6,399,396 B1) discloses in Fig. 1C a structure suitable for compressed loading of fluid from one substrate to another. In this case, the fluid, 13 is pushed out first rather than immersing the protruding tip inside as in the current invention. Karg et al. disclose an integrated metering tap with

various moving parts for microvolume liquid dispensing. The structural features are significantly different such as moving piston, spring, piston guides etc. Bjornson et al. (US Patent 6,103,199 and 6,284,113 B1) disclose a capillary electroflow apparatus. This apparatus consists of in Fig. 3 an array of sample receiving elements, 102 on a first plate, 100 and an array of microfluidic networks on another plate, 110. The structural features are not designed for two meniscus mixing, and require sealing between the two plates as shown in Fig. 8, which is not the feature proposed in the current application. Pfost et al. (US Patent 6,485,690 B1) show use of stacking of multiple plates with microchannel features for building of fluid processors. No protrusion structural features were addressed, no meniscus mixing were discussed as shown in Fig. 6 - 46. Features to move fluids in a valve configuration are discussed where moving fluid in one direction vs. another is important for fluid logic based applications. Dubrow et al. discuss a device that consists of plurality of ports connected to fluid channel network. The structural features require substantially planar surfaces without protrusions and tight seal between the two plates is necessary to drive the fluid from top plate to the bottom plate or vice versa. The structural features 106 and 114 of Fig. 1 are different from the current invention.

Conclusion

The prior art does not contain structural features to enable mixing of meniscus that are freely suspended in through-holes. The current application proposes such new structural elements and functional features, which allows new commercial applications.

The applicant respectfully requests to discuss the application over the phone to resolve the issues, which the Examiner

expressed interest in during earlier communication. Alex Freeman, Ph.D. cell phone number is 214-868-9101 and can be reached most of the time.

Conditional Request For Constructive Assistance

Applicant has amended the specification and claims of this application so that they are proper, definite, and define novel structure which is also unobvious. If, for any reason this application is not believed to be in full condition for allowance, applicant respectfully request the constructive assistance and suggestions of the Examiner pursuant to M.P.E.P 2173.02 and 707.07(j) in order that the undersigned can place this application in allowable condition as soon as possible and without the need for further proceedings.

Very respectfully,

Alex Freeman

-----------------Applicant Pro Se -------------------------

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2004 June 29

Alex Freeman